

REMARKS

Claims 1-8, 10, 11 and 25-34 are pending in the application.

CLAIM REJECTIONS

Rejection of claims under 35 U.S.C. § 112, first paragraph

Claims 1-8, 10, 11 and 25-34 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Specifically, although it is acknowledged that the Applicant has provided one example wherein an antisense oligonucleotide conjugated to a radioisotope does not exhibit uptake into the brain, it is alleged that Applicant has not provided a representative sample of the claimed genus of compounds that do not cross the blood-brain barrier.

A “representative number of species” means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus. *See, e.g.*, Rasmussen, 650 F.2d at 1214, 211 USPQ at 326-27 (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to “adheringly applying” because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered).

Although the targeting moiety of the various claimed species within the genus may vary, one of skill in the art would expect that the various species would not cross the blood/brain barrier without any additional showing or teaching otherwise. One of skill in the art is well aware that the blood/brain barrier strictly limits the ability of most agents to cross from the blood to the brain and very few effective delivery systems exist for the delivery of therapeutic molecules across this barrier. Thus, there is no substantial variation within the genus as regards the ability of the various species to cross the blood/brain barrier. Accordingly, the written description has been met by the detailed disclosure of the antisense oligonucleotide conjugated to a radioisotope.

Applicants respectfully request the withdrawal of the rejection for lack of written description.

Rejection of claims under 35 U.S.C. § 102(b) over Kuijpers et al.

Claims 1, 4, 5, 8, 10, 11, 25-28, 30-32 and 34 are rejected under 35 U.S.C. § 102(b) over Kuijpers et al. (EP 0 490 434).

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (emphasis added).

Kuijpers et al. is silent with regard to the ability of the disclosed constructs to cross the blood/brain barrier. The Examiner improperly relies on other references in an attempt to remedy this deficiency in the teaching of Kuijpers et al. However, Kuijpers et al. simply does not teach or suggest all of the limitations of claims 1, 4, 5, 8, 10, 11, 25-28, 30-32 and 34.

Applicants respectfully request the withdrawal of the rejection over Kuijpers et al. (EP 0 490 434).

Rejection of claims under 35 U.S.C. § 102(e) over Kayyem et al.

Claims 1-3 and 5-7 are rejected under 35 U.S.C. § 102(e) over Kayyem et al. (U.S. 6,232,295).

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (emphasis added).

Kayyem et al. is silent with regard to the ability of the disclosed constructs to cross the blood/brain barrier. The Examiner improperly relies on other references in an attempt to remedy this deficiency in the teaching of Kuijpers et al. However, Kayyem et al. simply does not teach or suggest all of the limitations of claims 1-3 and 5-7.

Applicants respectfully request the withdrawal of the rejection over Kayyem et al. (U.S. 6,232,295).

Rejection of claims under 35 U.S.C. § 103(a) over primary reference Kuijpers et al.

Claims 1, 4, 5, 8, 10, 11 and 25-34 are rejected under 35 U.S.C. § 103(a) as obvious over Kuijpers et al. (EP 0 490 434) and further in view of Gewirtz et al. (U.S. 5,098,890) and Low et al. (U.S. 5,994,320).

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Moreover, when a combination of references are used to establish a *prima facie* case of obviousness, the Examiner must present evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. See, e.g., *Carella v. Starlight Archery*, 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986); and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985). Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations (M.P.E.P. 2143).

The Examiner has not set forth any motivation to combine these references and hence has not established a *prima facie* case of obviousness. Moreover, even if there were motivation to combine the references, the combination does not teach or suggest each and every element of the claims.

Specifically, Kuijpers et al. is silent with regard to the ability of the disclosed constructs to cross the blood/brain barrier. Gerwitz et al. and Low et al. do not teach or suggest that the constructs disclosed in Kuijpers et al. do not cross the blood/brain barrier. Accordingly, the

combination does not teach or suggest each and every element of the claims, and the Examiner has not established a *prima facie* case of obviousness using these references.

Applicants respectfully request reconsideration and withdrawal of the rejection for obviousness.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims now pending are in condition for allowance, and notification of such is respectfully requested.

If, for any reason, a telephonic conference with the Applicants would be helpful in expediting prosecution of the instant application, the Examiner is invited to call Applicants' Agent at the telephone number provided below.


Respectfully submitted,

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June 22, 2006

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